delta T cell proliferation, phenotype, TCR repertoire and function to PB gamma delta T cells when culturing cells with the NBP, Zometa (zoledronic acid), and IL-2. Fourteen days in culture resulted in significant fold increase in the proliferation of gamma delta T cells and in the percent of lymphocytes in both sample types. PB gamma delta T cells proliferated more robustly than CB with a 288.60 versus 21.32 fold increase, respectively. Additionally, in freshly isolated samples, CB gamma delta T cells comprised an average of 1.404% of the lymphocyte population, which was similar to PB gamma delta T cells, with an average of 2.319%. However, by day 14, PB gamma delta T cells increased to 70.15% of lymphocytes whereas CB gamma delta T cells increased to 12.49%. Phenotypically, we also examined TCRγ9 and TCRδ2 expression and found that the TCRγ9δ2 was a common clone in freshly isolated PB gamma delta T cells, which predominated after 14 days in culture. However, while the TCRγ9δ2 variant was present in CB gamma delta T cells, it was low before and after culture, suggesting that Zometa may not stimulate gamma delta T cells in CB the same as PB. The memory subsets of freshly isolated gamma delta T cells were similar for CB and PB. Yet following culture, PB gamma delta T cells were mostly CD45RO+ memory cells, specifically effector or central memory subsets, with significantly fewer CD45RA+ naïve cells, whereas more CB gamma delta T cells were of the intermediate CD45RA+CD45RO+ naïve subset. In addition, we also observed that memory status corresponded with the TCR variant; more Vγ9 and Vδ2 cells were memory cells and Vδ1 cells were mostly naïve. Functionally, PB and CB gamma delta T cells had distinct cytokine secretion profiles both before and after culture. PB gamma delta T cells secreted more IFNγ and TNFα after culture, while CB gamma delta T cells secreted more IL-10 and RANTES. As limited TCRγδ phenotypic reagents are available, we developed a single cell PCR assay for genotypic analysis of the TCRγδ repertoire. PCR analysis suggests that the TCRγδ repertoire of freshly isolated cells is diverse in both samples types, with more variation among the CB gamma delta T cells, while TCRγ9δ2 is most prevalent in PB. Further analysis of the variant subsets is warranted and may give insight into how each of these receptor pairings affects gamma delta T cell function.

SUPPORTIVE CARE

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The Role of Tuberculin Skin Test As a Guide to Preventive Chemotherapy for Latent Tuberculosis Infection in Hematopoietic Stem Cell Transplantation in a Region with Intermediate Prevalence and Routine BCG Vaccination: A Preliminary Report from Turkey

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Turkey is a country with intermediate tuberculosis (TB) prevalence (24 cases per 100,000 population) where BCG vaccination is mandatory. Immunocompromised patients are at risk for TB infection. However, tuberculin skin test (TST) has limitations in immunocompromised patients while diagnosing latent TB infection (LTBI) and commencing isoniazid (INH) chemoprophylaxis. After 2000 consensus statements recommended INH prophylaxis in higher risk patients with a cut-off TST value of 5 mm. This retrospective study was conducted to determine the frequency of TB in HSCT recipients and the role of chemoprophylaxis with different cut-off values of TST (<5 mm, 5 to 10 mm, 10 to 20 mm, and ≥20 mm) in a region with intermediate TB prevalence.

Table
Distribution of BCG scar positivity and presence of INH prophylaxis with respect to TST values

	Autologous HSCT	Allogeneic HSCT
	N=320	N=272
TST value	Positive BCG scar/INH prophylaxis/total # of patients	Positive BCG scar/INH prophylaxis/total # of patients
0-4, 9 mm	68/13 /153	70/10/ 137
5- 9, 9 mm	21/14/ 37	24/16/ 33
10- 19, 9 mm	53/56/ 87	31/29/ 57
≥ 20 mm	5/9/ 17	7/7/ 8
data not available	26	37

Patients and Methods: Five hundred and ninety two patients [320 (54 %) autologous and 272 (46 %) allogeneic] transplanted at our center between September 2003 and July 2014 and survived for ≥100 days post-transplantation were included. The median age was 51 years-old (range 16-71) in autologous and 29 years-old (range 15-64) in allogeneic HSCT recipients. The decision to initiate INH prophylaxis was usually based on universal guidelines however modifications were also made at the discretion of the pulmonologist responsible for the pre-transplantation consultation or the new released guidelines. Anergy was defined as any reaction size of 0 to 2 mm in diameter.

Results: BCG scar data was available in 148 of 320 autologous (46.3 %) and 133 of 272 (48.9 %) allogeneic HSCT recipients. Distribution of positive BCG scar and INH prophylaxis with respect to TST values are given in table. Anergy was detected in 141 (44.1 %) of autologous and 124 (45.7 %) of allogeneic HSCT recipients. Positive BCG vaccination scar data was available in 47% of anergic patients. Ninety-two (28.8%) of autologous and 64 (23.5 %) of allogeneic HSCT recipients received INH prophylaxis. None of the allogeneic HSCT recipients and 1 in 320 (0.3 %) patients in autologous HSCT developed TB. This patient was TST anergic prior to transplantation and was not on chemoprophylaxis.

Conclusion: Our data showed low frequency of TB after HSCT despite variable chemoprophylaxis practices. Recent guidelines recommended reduction of TST threshold to 5 mm in higher risk patients. However our results suggest that these general guidelines do not apply to all patients and all regions.

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Nasal Endoscopy in the Evaluation of Prolonged Febrile Events in Children Undergoing Hematopoietic Stem Cell Transplantation

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Background: Early detection and treatment of fungal sinusitis is critical in the successful treatment of these

infections. Radiographic evaluations such as sinus CTs have been shown to be unhelpful in the diagnosis of fungal disease. We therefore initiated the practice of nasal endoscopy as part of our evaluation of HSCT patients who had prolonged fever.

Methods: We performed a retrospective review of all children who underwent HSCT at our institution from January 2011 until June 2014. Children were identified who underwent nasal endoscopy after a minimum of three days of fever despite the initiation of broad-spectrum antibiotics and who had negative bacterial blood cultures. The results of the endoscopy and any cultures obtained were reviewed. Demographic, clinical, microbiologic, management and outcome data were collected.

Results: A total of 44 nasal endoscopies were performed in 42 children. Three of the children had positive nasal endoscopies. Two were asymptomatic and were found to have suspicious lesions which were subsequently biopsied. These were found to be positive for *Fusarium spp* and *Rhizopus spp*. The third had rapid development of eye swelling and sinus pain and was found to have *Rhizopus spp*. The three children were then treated with aggressive serial debridement and initiation of multiagent antifungal therapy. All three of the children survived their fungal infection although one remains on antifungal therapy. Mild discomfort during the procedure was the only adverse event related to the use of endoscopy reported in this patient group. In those with a negative endoscopy, there were no children who subsequently developed fungal sinus disease. Three of these patients were later identified with a fungal infection at other sites: one had *bipolaris spp* of the skin, one had *Aspergillus flavus* isolated from an endotracheal tube aspirate and one had disseminated *Histoplasmosis capsulatum* isolated on post-mortem examination.

Conclusions: We conclude that nasal endoscopy is safe and effective in the evaluation of pediatric HSCT patients as part of the evaluation of prolonged fever to rule out fungal sinusitis. Early detection of fungal sinusitis by nasal endoscopy and aggressive surgical and antifungal therapy may improve the survival of HSCT patients.

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No Evidence of a Drug-Drug Interaction Between Letermovir (MK-8228) and Mycophenolate Mofetil

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Introduction: Letermovir (MK-8228) is a potent, once-daily inhibitor of the cytomegalovirus (CMV) terminase complex that is being developed for the prophylaxis of CMV infection in transplant patients. This study evaluated the pharmacokinetic interactions, safety and tolerability of letermovir when coadministered in healthy subjects with mycophenolate mofetil (MMF), which is the morpholinoethyl ester prodrug of mycophenolic acid (MPA).

Materials & Methods: This was an open label trial in 14 healthy female subjects that explored the pharmacokidsnetic parameters of a single 1 mg oral dose of MMF administered alone on day 1 and administered on day 12 with letermovir given orally as 480 mg once daily from day 8 and continued through day 16. Letermovir pharmacokinetics were assessed at single dose (day 5) and at steady state on day 12 (with MMF) and on day 16 (alone following MMF washout).

Results: Coadministration of a single dose of 1 mg of MMF with 480 mg daily letermovir at steady state had no effect on the pharmacokinetics of MPA. The MPA $AUC_{0\text{-inf}}$ and C_{max} geometric mean ratios (GMRs) [90% confidence interval] for the comparison (MMF with letermovir/MMF alone) were 1.08 [0.96, 1.21] and 0.96 [0.81, 1.13], respectively. Coadministration of 480 mg daily letermovir at steady state with a single dose of 1 mg MMF has no clinically meaningful effect on the pharmacokinetics of letermovir with $AUC_{0\text{-}24}$ and Cmax GMR of 1.18 [1.04, 1.33] and 1.11 [0.92, 1.35], respectively. The letermovir geometric mean accumulation ratio (Day 16/Day 5) and 95% CI were 1.13 [0.90, 1.42] for $AUC_{0\text{-}24}$ and 1.01 [0.79, 1.28] for C_{max}, indicating that accumulation of letermovir when administered as daily doses is minimal. All related AEs were reported as mild in severity and resolved. Following coadministration of letermovir and MMF, no clinically meaningful changes were observed in clinical laboratory values, vital signs, ECG or physical exam results.

Conclusions: Multiple dose administration of 480 mg letermovir daily with a single dose of 1 mg MMF was generally well tolerated by the healthy subjects in this study. Co-administration of letermovir with MMF had no clinically meaningful effect on the PK of letermovir or MMF. Letermovir and MMF may be coadministered without dose adjustment.

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Autoimmune Hemolysis (AH) & Immune Thrombocytopenic Purpura (ITP) after Cord Blood Transplantation (CBT) May be Life-Threatening & Warrant Early Therapy with Rituximab

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Introduction: While AH & ITP are recognized after CBT, the incidence, severity, treatment response, & prognosis of these complications is not established.

Methods: We evaluated AH/ITP in a day 100 landmark analysis of 152 double-unit CBT recipients (median age 38 years, range 0.9-70) who were transplanted for hematologic malignancies, engrafted & disease-free.

Results: Nine patients [median age 42 years (range 2-54), median follow-up 50.6 months (range 7.6-105.4) have developed autoimmune cytopenias (7 AH, 1 ITP, 1 both) for a 6% (95%CI: 3-11) 3-year cumulative incidence [median onset 8.6 months (range 5.8-24.5), Figure]. Six patients had severe disease (Hb < 6 gm/dl &/or platelets < 20). Their lowest counts (Hb 2.6-6.8 & platelets 0-4) were a median of 1 day (range 0-94) after diagnosis. Six had grade II-IV acute GVHD prior to AH/ITP, and all 9 patients developed AH/ITP in the context of immunosuppression taper. There was no association between AH/ITP and age, diagnosis, regimen intensity, or recipient CMV serostatus. Treatment in the first week was IVIg/corticosteroids/rituximab in 3 patients, whereas CSA dose was increased in 1, 2 had IVIg only, 2